REMARKS

Detailed Action

A. Information Disclosure Statement

Applicant acknowledges that the Information Disclosure Statement (IDS) has been considered. The Examiner further states that not all the cited references were available and hence were not considered.

B. Election/Restriction

Applicant acknowledges that the Examiner states that claims 1-32 are pending and that claims 7-32 have been withdrawn. The Examiner states that claims 1-6 are currently under examination.

C. Priority

The Examiner acknowledges Applicant's claim for the benefit of the prior-filed application, however, states that Applicant has not complied with one or more conditions for receiving the benefit of the earlier filing date "under 35 U.S.C. [1]." Because it is unclear which section of the code the Examiner is referring to with "[1]," we assume 35 U.S.C. § 120 unless notified otherwise. The Examiner cites *Transco Products, Inc. v. Performance Contracting, Inc.* for the proposition that the disclosure of an invention in a parent application and in a later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. § 112, and states that because the prior-filed application does not disclose oligoribonucleotides (ORN) with a molecular weight of less than 10 kDa or sequences set forth in SEQ ID NOS: 1-3, the filing date of the instant application will consequently be used for prior art purposes.

Applicant traverses. Applicant asserts this application was filed pursuant to 37 CFR § 1.53(b) as a continuation-in-part, defined and described in section 201.08 of the MPEP as "adding matter not disclosed in the said earlier nonprovisional application." Therefore, the new disclosure of SEQ ID NOS: 1-3 and oligoribonucleotides (ORN) with a molecular weight less than 10kDa is appropriate for this type of application, especially considering that Applicant has satisfied all other requirements of 37 CFR § 1.53(b) and 35 U.S.C. § 120. Furthermore, section 201.08 goes on to state "[u]nless the filing date of the earlier nonprovisional application is actually needed, for example, in the case of an interference or to overcome a reference, there is

no need for the Office to make a determination as to whether the requirement of 35 § U.S.C. 120, that the earlier nonprovisional application discloses the invention of the second application in the manner provided by the first paragraph of 35 U.S.C. § 112, is met...." Applicant submits that the earlier filing date is not "actually needed" in this case in the sense of an interference proceeding or overcoming a reference, and further submits that all other requirements described under 35 U.S.C. § 120 (and as described in MPEP Section 201.08) have been fulfilled. Applicant therefore respectfully requests that the filing date of the instant application (3-15-2004) not be used for prior art purposes.

Provisional Double Patenting

The Examiner rejects claims 1-3 and 6 provisionally under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-21 of copending U.S. Application No. 11/284,517. The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because "both claim sets are drawn to oligoribonucleotides (ORN) from bacteria with a molecular weight of less than 10kDa and both sets encompass ORNs that are 1-30 nucleotides in length".

Applicant is herein submitting a Terminal Disclaimer in compliance with 37 C.F.R. § 1.321(c), which disclaims any term of a patent issuing from this application which would extend beyond the term of copending U.S. Application No. 11/284,517. Therefore, Applicant submits that the claims are in proper form for allowance and respectfully request reconsideration and withdrawal of the provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 112, second paragraph

Claims 5 and 6 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For claim 6, the Examiner points to the language "the ORN consists of signature sequences as defined in the definitions and only found in microbes as defined in the definitions" as being vague and indefinite, and furthermore states that it is unclear what is meant by the said term as the specification provides no listing of said "signature sequences" or sequences found only in microbes.

Applicant respectfully traverses this rejection. The disclosure adequately defines what is meant by "signature sequences" in microbes. Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) the content of the particular application disclosure; (B) the teachings of the prior art; and (C) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. (*See* MPEP Section 2173.02). Looking to the disclosure, "signature sequence" is specifically described in the "Definitions" section of the specification as meaning "oligoribosomal nucleotides that contain sequences found only in the ribosomes of specific orders, families, genera or species of microbes," and then further lists references that can be consulted for example listings of such sequences in specific microbes. (Specification, p. 5, para. 0057). Therefore, in light of the disclosure of a definition for the term "signature sequence" accompanied by references in the art, one of ordinary skill in the art would understand what a signature sequence means in claim 6, and which microbes such a sequence would be found in, without having to see every potential sequence or microbe explicitly listed in the specification.

The Examiner has also pointed out that claim 5 is rendered vague and indefinite by the use of the phrase "consisting of a base sequence selected from the group consisting of..." because "consisting of" suggests the language is closed while "base sequence" suggests that the claimed ORN contains more than the recited base sequence.

Although not acceding to the Examiner's rejection, in an effort to expedite prosecution Applicant has now amended claim 5 to read "an oligoribonucleotide (ORN) from bacteria, comprising a base sequence selected from the group consisting of" which clarifies that the claim is intended to be open with regard to the sequence of the ORN.

In light of the above amendments and remarks, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

Claim Rejections - 35 USC § 102

Claims 1-4 and 6 stand rejected under 35 U.S.C. § 102(b) as being anticipated by both Krieg et al. and Schwartz et al. The Examiner mentions that the burden is on the Applicant to show the distinction between material, structural, and functional characteristics of the claimed composition over the prior art of these references.

Applicant traverses. However, before addressing this burden, Applicant would like to mention that with regard to Schwartz, the Examiner has pointed to a SEQ ID NO: 68 as being an identical sequence to SEQ ID NO: 3 in claim 5. Nonetheless, no such sequence could be found after diligent searching for this sequence in every electronic version of the publication available on the web, and after searching for bits of the claimed sequences in the publication to make sure the Examiner didn't mean to refer to some other sequence in the publication or one of Applicant's other claimed sequences. Therefore, Applicant is unfortunately unable to fully respond to this aspect of the Examiner's rejection. Nonetheless, Applicant feels this uncertainty is inconsequential to the following arguments with regard to material, structural, and functional differences.

First, the Examiner states that Krieg et al. disclose immunostimulatory nucleic acids in the abstract, and that said nucleic acids have the same stimulatory effect as "bacterial proteins" (referring to page 1, lines 13-15). However, Krieg contains no mention of bacterial proteins, but rather speaks of the immune stimulatory effects of "bacterial DNA." Moreover, the Examiner states that Krieg et al. disclose an oligoribonucleotide (ORN) labeled SEQ ID NO: 391 that is identical to claimed SEQ ID NO: 3, however, SEQ ID NO: 391 is not an ORN but rather an oligodeoxynucleotide (ODN), which Krieg states can mimic the immunostimulatory effects of bacterial DNA. Therefore, Krieg et al. only discloses immunostimulatory ODNs, which are materially and structurally different from ORNs due to the presence of uracil instead of thymine, and the presence of a 2' OH group where none is present in ODNs. Similarly, Schwartz et al. also contains no mention of any ORNs and specifically lists sequences of ODNs in its disclosure. Applicant thus assumes that the SEQ ID NO: 68 the Examiner intended to refer to would have been ODN as well, and not an ORN.

Second, it should be noted that ORNs have different stoichiometric properties than ODNs by virtue of the differences mentioned above. The specification indicates that this difference in properties is of strong consequence on the function of these molecules in relation to a host organism's immune system. For example, although it has been shown by Krieg et al. that ODNs of 4-10 deoxynucleotides which contain one or two CpG motifs have an immunostimulatory effect, they have also discovered that such molecules are toxic. (Specification, p. 4, para. 0046)(citing Krieg, A M, et al., 1995, CpG Motifs in Bacterial DNA Trigger Direct B-cell

Activation, Nature 374: 546-9). Specifically, high doses of ODNs were found to be toxic and increase the animal's sensitivity to endotoxin and cause septic shock. (Specification, p. 8, para. 0094). However, neither Krieg nor Schwartz made the discovery of the Applicant that ORNs lack the toxic effects of ODNs but retain the immunostimulatory effect, and therefore can be safely administered to animals. (See, e.g., Specification, p. 7, para. 0083, column 2). The fact that ODNs are toxic to the host organism whereas corresponding ORNs are not proves not only a strong functional difference between the two, but also that ORNs are structurally different enough from ODNs that an animal's immune system can recognize this difference. Additionally, the resistance of ORNs<10kDa to RNase suggests that the ORNs have unusual structures. (Specification, p. 2 para. 0018). Some may have substitutions on their bases (e.g., methyl and other groups) or may have two nucleotide strands held together by complementarity or folded back upon themselves. These unusual structural conditions leading to resistance to RNase are believed to be responsible for their stimulation and modulation of the immune system, and such structural conditions will likely vary between ODNs and ORNs due to their different stoichiometric properties.

Lastly, at the end of the discussion regarding Krieg et al., the Examiner states that the CpG motif disclosed by Krieg et al. is deemed to be the "signature sequence" of claim 6. This same exact statement with reference to Krieg et al. is also placed by the Examiner at the end of the discussion of Schwartz et al., therefore Applicant assumes unless notified otherwise that what was meant was the CpG motif disclosed by Schwartz et al. with regard to this part of the discussion. In either case, it is relevant that claim 6 is dependent upon claim 2, which is written to ORNs, not ODNs. As mentioned before, both Krieg and Schwartz et al. only disclose ODNs and neither contain any mention of the possibility of using ORNS. Therefore, neither disclosure is enabling for CpG motifs in the context of oligoribonucleotides. As described *supra*, oligodeoxynucleotides and oligoribonucleotides have important structural and functional differences with regard to immune system interaction and toxicity, and thus the references cited would have to show experimentation with ORNs in order to enable one skilled in the art to use such an invention to modulate or stimulate the immune system of an animal. It should be further noted the specification states that two examples of structures specific to microbes are known, the first being "signature sequences" of nucleotides known to occur uniquely in the ribosomes of

specific orders, families, genera or species of microbes, and the second being the sequences of nucleotides in DNA that contain the CpG motif in DNA at a much higher frequency in bacteria. (Specification, p. 2, para. 0019-0021). In other words, CpG motif-containing nucleotides are described as separate from the claimed "signature sequences" as defined in the specification. In fact, Krieg et al. disclose that nucleic acid sequences which do not contain CpG motifs can be immunostimulatory (p 2, lines 21-22), and therefore "signature sequences" do not have to inherently contain CpG motifs. However, if such signature sequences as defined in the specification did contain a CpG motif by chance, this would not exclude protection of such a sequence because neither Krieg nor Schwartz et al. enable this motif in ORNs.

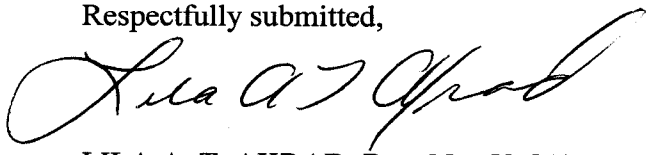
In light of the above, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection to claims 1-4 and 6 under 35 U.S.C. § 102 (b).

Conclusion

In conclusion, Applicant submits in light of the above amendments and remarks, the claims as amended are in a condition for allowance, and reconsideration is respectfully requested. If it is felt that it would aid in prosecution, the Examiner is invited to contact the undersigned at the number indicated to discuss any outstanding issues.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Respectfully submitted,



LILA A. T. AKRAD, Reg. No. 52,550
McKEE, VOORHEES & SEASE, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No: (515) 288-3667
Fax No: (515) 288-1338

CUSTOMER NO: 22885
Attorneys of Record

- LATA/JRC/bja/pw -